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Plaintiff In Propria Persona

UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA

DAVID BEHAR, M.D., on behalf of himself and his patients, Plaintiff, v. U.S. FOOD AND DRUG ADMINISTRATION; STEPHEN M. HAHN, M.D., in his official capacity as Commissioner of Food and Drugs; U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES; and ALEX M. AZAR II, in his official capacity as Secretary of Health and Human Services, Defendants.	**Civil Action No. _____**

COMPLAINT FOR DECLARATORY AND INJUNCTIVE RELIEF

Plaintiff DAVID BEHAR, M.D. ("Plaintiff") seeks declaratory and injunctive relief against the U.S. Department of Health and Human Services ("HHS"), its constituent agency, U.S. Food and Drug Administration ("FDA"), and their respective lead officers (collectively, "Defendants"), based on the following allegations.

NATURE OF THE ACTION

1. Plaintiff brings this action on behalf of himself and his patients seeking a declaration that the FDA's Risk Evaluation and Mitigation Strategies ("REMS") program

regarding clozapine, an extraordinarily effective antipsychotic drug, is unconstitutional. In addition, Plaintiff seeks an order enjoining the FDA from requiring a REMS for clozapine and/or remand to the FDA with instructions to remove the Clozapine REMS.

2. Under the FDA's current Clozapine REMS, in order to prescribe clozapine, a health care professional must be certified to do so. The Clozapine REMS further requires patients to be monitored for changes to their absolute neutrophil counts ("ANC") by submitting to weekly blood draws for the first four weeks and thereafter to bi-weekly blood draws. The motivation for this monitoring requirement is the fact that taking clozapine has led to agranulocytosis[1] and neutropenia[2] in 0.1% to 0.8% of patients, which may suppress the patient's immune system and make them susceptible to potentially fatal infection. Neutrophils cage up and destroy bacteria after getting a signal of any invasion of the body.

3. Given the low incidence of fatal side-effects, the blood monitoring requirement makes the Clozapine REMS oppressive and illegal. There are dozens of other FDA-approved prescription-only medications causing agranulocytosis and neutropenia at the same or higher incidence rates than clozapine. The FDA has not implemented a REMS for them. Clozapine REMS deters psychotic patients from taking clozapine due to the onerous blood monitoring requirement. There is an undue burden imposed upon patients by the Clozapine REMS. For those reasons, Plaintiff seeks a declaratory judgment holding that the Clozapine REMS is unconstitutional and ordering Defendants to decommission the program. Instead, health care professionals should use clinical judgment for treatment and monitoring of clozapine patients, as is the case for dozens of other medications having similar or worse side-effects.

[1] *Agranulocytosis*, also known as agranulosis or granulocytopenia, is an acute condition involving a severe and dangerous leukopenia (lowered white blood cell count), most commonly of neutrophils, and thus causing a neutropenia in the circulating blood.

[2] *Neutropenia* is an abnormally low count of neutrophils (a type of white blood cell) in the blood that fight bacteria.

The Monitoring Requirement Originated as a Medicare Fraud Scheme[3]

4. After decades of failed attempts, Sandoz was finally able to obtain FDA approval for clozapine. In 1975, nine patients in Finland died while taking clozapine due to agranulocytosis. Sandoz proposed to introduce clozapine to the US market with a mandatory blood monitoring regimen that is substantially the same as what exists under the Clozapine REMS today. Following Sandoz's obtaining FDA approval, there was massive public outcry owing to the exorbitant pricing imposed by Sandoz for the bundled mandatory blood testing and clozapine medication. On December 18, 1990, twenty-nine States and the District of Columbia filed suit against Sandoz in Federal Court for antitrust violations.

5. In late 1990, Sandoz published full-page advertisements in prominent newspapers declaring that they would unbundle the mandatory blood testing from the medication. However, Sandoz took no such action to implement their published promise. In May 1991, the Senate Subcommittee issued their ruling, finding that both the Sandoz clozapine monitoring plan and the states themselves were at fault for creating barriers to access. The ruling further ordered the state Medicaid programs to pay for clozapine and associated blood monitoring costs for all eligible patients. In addition, Sandoz was ordered to pay $30 million to settle the class action lawsuit. It is clear from this history that the introduction of clozapine into the US market has its origins in a Medicare fraud scheme under which Sandoz attempted to exact payment at an exorbitant rate both for the mandatory blood testing that it had imposed in order to vitiate concerns about the side-effects of clozapine and for clozapine itself. As such, the current Clozapine REMS has its roots in criminal fraud. Indeed, the official slogan of the Clozapine REMS is **No Blood, No Drug™**— evidencing an inhumane, inflexible, extortionist, unconstitutional restriction on access

[3] Crilly, J (2007). The history of clozapine and its emergence in the US market: a review and analysis. *History of Psychiatry* 18(1): 39-60.

to the medication, possibly contradicting the judgment of the physician who knows the patient well. It also constitutes a requirement that patients pay for blood testing in order to be prescribed the medication even if blood testing isn't medically necessary. A medical procedure that is not medically necessary is medical fraud.

6. A REMS is a required risk management plan that can include one or more elements to ensure that the benefits of a drug outweigh its risks.[4] If the FDA determines that a REMS is necessary, they may require one or more REMS elements and may also require elements to assure safe use ("ETASU").[5] All REMS should include one or more overall goals, and if the REMS has ETASU, the REMS must include one or more goals to mitigate a specific serious risk listed in the labeling of the drug and for which the ETASU is required.[6] Section 505-1(a)(1) of the FD&C Act as implemented in the Food and Drug Administration Amendments Act of 2007 ("FDAAA") requires the FDA to consider the following six factors in making decisions about whether to require a REMS:

a) The seriousness of any known or potential adverse events that may be related to the drug and the background incidence of such events in the population likely to use the drug;

b) The expected benefit of the drug with respect to the disease or condition;

c) The seriousness of the disease or condition that is to be treated with the drug;

d) Whether the drug is a new molecular entity;

e) The expected or actual duration of treatment with the drug; and

f) The estimated size of the population likely to use the drug.

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[4] *See* FD&C Act §§ 505-1(e) and 505-1(f).

[5] *See* FD&C Act § 505-1(e)(3).

[6] *Id.*

7. The FDA characterized clozapine as an ETASU in implementing the Clozapine REMS, with the specific "serious risk" being agranulocytosis. The FDA first required a REMS for clozapine in September 2015, applicable to all clozapine medicines on the market and requiring patient monitoring via a centralized system to monitor and manage clozapine-induced neutropenia.

8. Congress imposed several additional requirements to ensure that the FDA appropriately balances an inherently toxic drug's benefits against its "serious risks." The ETASU requirements must "be *commensurate* with the specific serious risk[s]" listed in the drugs' labeling, and may "not be *unduly burdensome* on patient access to the drug, considering the particular . . . patients who have difficulty accessing health care (such as patients in rural or medically underserved areas)." 21 U.S.C. §§ 355-1(f)(2)(A), (C) (emphases added). In addition, "to the extent practicable, so as to minimize the burden on the health care delivery system," ETASU must "conform with elements to assure safe use for other drugs with similar serious risks." *Id.* § 355-1(f)(2)(D).

9. A modification or removal of a REMS may be initiated by a "responsible person" (i.e., the drug's sponsor) or by the Secretary of HHS, who may "require a responsible person to submit a proposed modification to the strategy." *Id.* §§ 355-1(g)(4)(A), (B).

10. In addition, the Secretary of HHS must "periodically evaluate, for 1 or more drugs, the [ETASU] to assess whether the elements (i) assure safe use of the drug; (ii) are not unduly burdensome on patient access to the drug; and (iii) to the extent practicable, minimize the burden on the health care delivery system." *Id.* § 355-1(f)(5)(B). Then, "considering such input and evaluations," the agency must "modify [ETASU] for 1 or more drugs as appropriate." *Id*. § 355-1(f)(5)(C).

11. On February 28, 2019, changes to the Clozapine REMS took effect requiring prescribers and pharmacies to be certified under the Clozapine REMS in order to prescribe or dispense clozapine. This action constitutes final agency action for which Plaintiff and Plaintiff's patients have no other adequate remedy within the meaning of 5 U.S.C. § 704.

12. The FDA's reauthorization of the Clozapine REMS and other agency action and inaction described herein is contrary to Plaintiff's and Plaintiff's patients' constitutional rights, including their rights under the Fifth Amendment to the U.S. Constitution, in violation of 5 U.S.C. § 706(2)(B).

A. Seriousness of Known or Potential Adverse Events and Background Incidence

13. Clozapine carries a black box warning for drug-induced agranulocytosis. Without monitoring, agranulocytosis occurs during the first few months of treatment in about 1% of patients who take clozapine.[7] The risk of agranulocytosis is highest around three months into treatment after which time the risk decreases markedly to less than 0.01% after one year.[8] Due to this risk of agranulocytosis, the current package insert for clozapine requires withholding delivery of clozapine to anyone with an absolute neutrophil count (ANC) below 2000/mm^3. If a mild granulocytopenia has taken place (2000/mm^3 > ANC ≥ 1500/mm^3), then biweekly blood tests are required until the counts rise to the acceptable threshold level. Moderate leukopenia or moderate granulocytopenia require cessation of clozapine therapy and twice-weekly blood tests until the patient has reached "mild granulocytopenia" levels. With severe granulocytopenia (ANC < 1000/mm^3), clozapine treatment must be permanently discontinued.

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[7] Baldessarini RJ, Tarazi FI (2006). Pharmacotherapy of Psychosis and Maa. In Laurence Brunton, John Lazo, Keith Parker (eds.). *Goodman & Gilman's The Pharmacological Basis of Therapeutics* (11th ed.).

[8] Alvir JM, Lieberman JA, Safferman AZ, Schwimmer JL, Schaaf JA (1993). Clozapine-induced agranulocytosis. Incidence and risk factors in the United States. *N. Engl. J Med.* 329(3):162–167.

14. In contrast, there are over seventy other prescription medications that also carry a black box warning for drug-induced agranulocytosis or neutropenia but which are not subject to a REMS. In particular, Ibrance (palbociclib) has an incident rate of neutropenia of 80% and yet defers monitoring to the discretion of the health care provider. Ibrance is a medication for treatment of HR-positive and HER2-negative breast cancer. While Ibrance has been approved for treatment of both women and men, the incidence of breast cancer is 101 times more common in women than in men.

15. Likewise, methicillin, a semisynthetic penicillin, has a 2% to 8% incidence of agranulocytosis but has no comparable safety monitoring.

16. Consequently, the monitoring requirement for clozapine cannot rationally be justified by the incidence of agranulocytosis.

17. Neutropenia most often is not confirmed on a subsequent blood test. If it is confirmed, a low dose of lithium such as 300 mg (for ten cents) will stimulate the bone marrow to make more. If lithium does not end the neutropenia, more expensive medications are available from hematologists. Clozapine should not be stopped as required by the Clozapine REMS, even in the face of neutropenia. The psychiatric consequences are too drastic, and the multiple bone marrow stimulants are effective at restoring the neutrophil counts.

B. Benefits of Clozapine

18. Clozapine is an atypical, second-generation antipsychotic drug indicated for the management of severely ill schizophrenic patients who fail to respond adequately to standard drug treatment for schizophrenia, either because of insufficient effectiveness or the inability to achieve an effective dose due to intolerable adverse effects from those drugs. Clozapine is traditionally used as a "treatment of last resort" for patients who have failed to improve after two

adequate trials of other drugs. Approximately 1.5 million people in the United States suffer from schizophrenia, and up to one third of patients with schizophrenia develop treatment resistance and are unresponsive to first-line antipsychotic therapy.[9] There is no other antipsychotic that has comparable efficacy to clozapine in the treatment of resistant schizophrenia.[10] The FDA approved the use of clozapine in such contexts in 1989. The National Institute of Mental Health notes that clozapine is "a very effective medication that treats psychotic symptoms, hallucinations, breaks with reality, such as when a person believes he or she is the president."[11]

19. Since 2002, clozapine has also had an FDA-approved indication for the treatment of recurrent suicidal behavior in schizophrenia and schizoaffective disorder. It is the best-studied medication for specific beneficial effects on suicidal behaviors. Analysis of clozapine patients has shown a 75% to 82% reduction in mortality, due primarily to a decrease in suicide risk.[12] Other analyses have found a 67% reduction in risk for suicide attempts.[13]

20. The world is currently in the midst of a global pandemic caused by the novel coronavirus, COVID-19. COVID-19 infection is associated with neurological conditions including acute ischemic stroke, headache, dizziness, ataxia and seizures.[14] A recent review of the impact of COVID-19 on the brain shows that neurological conditions are present in about

[9] Mistry H, Osborn D (2011). Underuse of clozapine in treatment-resistant schizophrenia. *Adv. in Psych. Treatment*, Vol. 17, Issue 4, pp. 250-255.

[10] Kelly DL, Kreyenbuhl J, Dixon L, Love RC, Medoff D, Conley RR (2007). Clozapine underutilization and discontinuation in African Americans due to leucopenia. *Schizophr. Bull.* 33(5): 1221-1224.

[11] National Institutes of Health (2010). Mental Health Medications. NIH Pub. No. 12-3929, p. 2.

[12] Anderson AE (1999). Using medical information psychotherapeutically. *Eating Disorders: A Guide to Medical Care and Complications.* Mehler PS, Andersen AE, eds. Johns Hopkins University Press, Baltimore, pp. 192-201.

[13] Commerford MC, Licinio J, Halmi KA (1997). Guidelines for Discharging Eating Disorder Patients. *Eating Disorders: The Journal of Treatment and Prevention* 5:69-74.

[14] Asadi-Pooya AA, Simani L (2020). Central nervous system manifestations of COVID-19: a systematic review. *J Neural Sci* 413: 116832.

25% of COVID-19 patients.[15] Many recovering COVID-19 patients have physical symptoms including pain for a long time.[16] Neurological disorders such as ischemic stroke, headache and seizures are associated with suicidal behavior.[17] Physical symptoms, especially pain also increase suicide risk.[18,19] From 1999 through 2017, the age-adjusted suicide rate in the United States grew 33%, from 10.5 to 14.0 per 100,000. There is a high probability that suicide rates will increase significantly due to the pandemic.[20] Many outpatient labs were closed during the COVID-19 pandemic. As a result, the Clozapine REMS temporarily waived the blood test requirement on an individual basis. No increase in morbidity from neutropenia resulted during this natural experiment of ceasing the Clozapine REMS.

21. Off-label beneficial uses of clozapine represent half of all clozapine prescriptions. These uses include treatment of the following: mania, intermittent explosive disorder, post-traumatic stress disorder, and psychosis caused by medication for Parkinson's disease. All uses of clozapine are unified by the severity and treatment-resistance of the patients for whom it is prescribed. It is beyond cavil that, therapeutically, clozapine is and has been a stellar success.[21]

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[15] *Id*.

[16] D'Ambrosio A (EPub 13 May 2020). COVID-19 sequelae can linger for weeks. *MedPage Today*.

[17] Hudzik TJ, Marek GJ (2014). Neurological disease and suicidal behavior. In: Cannon KE, Hudik TJ, eds. *Suicide: Phenomenology and Neurobiology.* Springer Int'l Publishing, Cham, Switzerland.

[18] Sher L (EPub 20 June 2019). Resilience as a focus of suicide research and prevention. *Acta Psychiatr Scand* 140:169-80.

[19] Ahmedani BK, Peterson EL, Hu Y, Rossom RC, Lynch F, Lu CY, et al. (EPub 12 June 2017). Major physical health conditions and risk of suicide. *Am. J Prev Med* 53: 308-315.

[20] Sher, L (EPub 30 June 2020). The impact of the COVID-19 pandemic on suicide rates. *QJM: An International Journal of Medicine*.

[21] Newman WJ, Newman BW (2016). Rediscovering clozapine: Clinically relevant off-label uses. *Current Psychiatry* 15: 51-61.

C. Seriousness of Condition that is Treated with Clozapine

22. Agranulocytosis is an acute condition involving severe and dangerous leukopenia, most commonly of neutrophils, and thus causing neutropenia in the circulating blood.[22] This may lead to a suppression of the immune system, subjecting the patient to an increased risk of bacterial infection.

D. Clozapine is Not a New Molecular Entity

23. Clozapine was first identified in 1959 as one of a group of tricyclic compounds based on the chemical structure of the antidepressant imipramine that were synthesized the prior year by Swiss pharmaceutical company Wander AG. Sandoz acquired Wander AG in 1967, and in the early 1970s, clozapine began clinical trials in the US. FDA approval was obtained in or around 1990, and clozapine (under the brand name "Clozaril") entered the US market on February 5, 1990. Hence, clozapine cannot be considered to be a new molecular entity.

E. Expected Duration of Treatment with Clozapine

24. Patients treated with clozapine are expected to be on the medication for life.

F. Estimated Size of Population Likely to Use Clozapine

25. There are approximately 1.5 million people in the US that suffer from schizophrenia. Of these, about 30% are treatment resistant.[23] *Between 19% and 28% of schizophrenics who are treatment resistant and who would benefit from clozapine refuse to take the medication because of the Clozapine REMS' mandatory weekly blood testing.*[24] This may be

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[22] *Stedman Medical Dictionary.*

[23] Mistry H, Osborn D (2011). Underuse of clozapine in treatment-resistant schizophrenia. *Adv. in Psych. Treatment*, Vol. 17, Issue 4, pp. 250-255.

[24] Taylor D, *et al*. (2000). Clozapine -- a survey of patient perceptions. *The Psychiatrist* 24(12): 450-452.

attributed to trypanophobia[25] and to the fact that these patients are, by and large, the most paranoid, dangerous schizophrenics and psychotics in the population. The net number of patients who do not take clozapine due to the existence of the Clozapine REMS is thus estimated to be between 85,000 and 126,000. *These treatment-resistant schizophrenics for whom clozapine represents the only medication effective in treating their condition represent a clear and present danger to society and to themselves.*

Sudden Interruption of Clozapine Treatment Can Be Catastrophic

26. Under the current regulations, patients may experience repeated, random interruptions in treatment of varying duration, depending on when their WBC and ANC counts rebound to "acceptable" levels. It is ironic that if infected, the counts will jump to high levels, and clozapine may again be dispensed.

27. The following have been reported as effects of sudden discontinuation of clozapine: bad flu-like symptoms with headaches and vomiting lasting a week; delirium; the return of original psychotic symptoms; the return of suicidal ideas; and abnormal movements ("These subjects had severe limb-axial and neck dystonias and dyskinesias 5 to 14 days after clozapine withdrawal. Two subjects were unable to ambulate and 1 had a lurching gait.") These are immediate, acute effects, which remit quickly with the resumption of clozapine.[26] These are

[25] *Trypanophobia* is the name for an extreme fear of medical procedures involving injections or hypodermic needles. It is estimated that at least 10% of American adults have a fear of needles, and it is likely that the actual number is larger since the most severe cases are never documented due to the tendency of the sufferer to avoid all medical treatment. *See* Hamilton, JG (1995). Needle Phobia – A Neglected Diagnosis. *J Family Practice* 41(2): 169-175.

[26] Ahmed S., Chengappa KN, Naudu VR, Baker RW, Parepally H, Schooler NR (1998). Clozapine withdrawal-emergent dystonias and dyskinesias: a case series. *J Clin. Psychiatry* 59(9): 472-477.

Stanilla JK, de Leon J, Simpson GM (1997). Clozapine withdrawal resulting in delirium with psychosis: a report of three cases. *J Clin. Psychiatry* 58(6): 252-255.

Miodownik C, Lerner V, Kibari A, Toder D, Cohen H (2006). The effect of sudden clozapine discontinuation on management of schizophrenic patients: a retrospective controlled study. *J Clin. Psychiatry* 67(8): 1204-1208.

the symptoms of physical withdrawal. The recurrence of psychosis (hearing voices, paranoia, and a formal thought disorder), impulsivity, and intense urges to hurt oneself and others are extremely serious.

28. The more disturbing consequence is evidence of brain damage necessitating higher doses and taking longer to work: "the discontinuation of clozapine treatment leads to a deterioration in the quality of remission, with a need for an increased dose of clozapine."[27] Duration of under-treatment also correlates with measurable losses of grey matter. A proper analogy would be the ease of treating a microscopic breast cancer lump versus a tumor the size of a baseball which has been allowed to grow untreated.

29. Interruption in clozapine treatment may also lead to relapse, in some cases with dramatic aggravation of the psychotic symptomatology, a phenomenon known as "supersensitivity" psychosis.[28] Treatment resistance to clozapine in prior clozapine responders has also been reported; patients whose clozapine treatments have been interrupted due to temporarily low WBC counts have experienced decreased effectiveness when treatment is resumed.[29]

30. Discontinuation of clozapine has also been found to have a marked negative impact on clinical status, including decreases in function and increases in time spent in mental facilities.[30] It is clear from these and other studies that the current regulations mandating

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[27] Bangalore SS, Gloria DD, Nutche J, Diwadkar VA, Prasad KM, Keshavan MS (EPub 3 April 2009). Untreated illness duration correlates with gray matter loss in first-episode psychoses. *Neuroreport*.

[28] Llorca PM, Penault F, Lançon C, Dufumier E, Vaiva G (1999). *Encephale* 25(6): 638-644.

[29] Grassi B, Ferrari R, Epifani M, Dragoni C, Cohen S, Scarone S (1999). Eur. Neuropsychopharmacol. 9(6): 479-481.

[30] Atkinson JM, Douglas-Hall P, Fischetti C, Sparshatt A, Taylor DM (2007). Outcome following clozapine discontinuation: a retrospective analysis. *J Clin. Psychiatry* 68(7): 1027-1030.

cessation of clozapine treatment based solely upon WBC and ANC counts without concern for other factors, including the potentially severe negative consequences to patients of such cessation are not sufficiently refined to be considered thoughtful, responsible regulations: in many published cases, patients have experienced severe consequences as a direct result of the current regulations, leaving those patients in a worse condition than they were before clozapine treatment began.

Motivation for the Complaint

31. The decommissioning of the Clozapine REMS will have great public benefit. "Given the high costs of medication discontinuation, rehospitalization and inadequate treatments for schizophrenia, the underutilization of clozapine in the United States is particularly noteworthy."[31] A positive verdict in the instant matter will have an immediate impact on those patients with treatment-resistant schizophrenia and schizoaffective disorder; Plaintiff finds it difficult to put into words how significant the increase in quality of life for those patients will be. The savings in terms of societal and social costs are difficult to quantify but would be significant. In addition, adopting these requests will decrease the disparity that currently exists with respect to the use of second-generation antipsychotics in the treatment of schizophrenia, which is an acute problem in the United States; as Defendant HHS noted, "'the combined costs of health inequalities and premature death in the United States were $1.24 trillion' between 2003 and 2006."[32] Finally, the demands herein are fully aligned with the HHS's goals under *Healthy People 2020* "to achieve health equity, eliminate disparities and improve the health of all

[31] Kelly, *supra.*

[32] Department of Health and Human Services (2011). HHS Action Plan to Reduce Racial and Ethnic Health Disparities [Internet]. p. 2. Available at https://minorityhealth.hhs.gov/npa/files/plans/hhs/hhs_plan_complete.pdf (Last accessed November 4, 2020.)

groups."[33] Clinical judgment may also require the testing for neutropenia after an unremitting infection, such as a sore throat, in between the required REMS testing. Individualized medical decisions are vastly superior to inflexible regulations; the latter may lead not only to over-testing but also to under-testing given the medical needs of a particular patient, the needs of which are known by the patient's doctor.

32. Discrimination in medicine is a medical practice that includes both differential treatment on the basis of a protected class (disparate-treatment discrimination) and treatment on the basis of inadequately justified factors that disadvantages a particular group (disparate-impact discrimination).[34] Disparate treatment involves intentional discrimination and is per se unconstitutional. Statistical disparity is sufficient for a legal showing of discrimination.[35] In contrast, a determination as to the legality of disparate-impact discrimination depends upon whether the practice is supported by a sufficiently compelling reason and whether alternative processes exist that would not give rise to disparities. Disparate-impact liability mandates the "removal of artificial, arbitrary, and unnecessary barriers . . ."[36]

33. In implementing the Clozapine REMS, Defendants violated the equal protection guarantee implicit in the Due Process Clause of the Fifth Amendment to the U.S. Constitution. The Clozapine REMS impermissibly discriminates based on a patient's disability, without a rational basis for this discrimination.

34. The current FDA regulations governing the use of clozapine are unconstitutional

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[33] *Id.* at p. 8.

[34] National Research Council (2004). *Measuring Racial Discrimination.* The National Academies Press, Washington, DC. p. 40. *Available at* http://www.nap.edu/catalog.php?record_id=10887 (Last accessed Feb. 20, 2012).

[35] *Texas Dept. of Housing and Community Affairs v. Inclusive Communities Project, Inc*., 576 US ____ (2015).

[36] *Griggs v. Duke Power Co*., 401 US 424, 431 (1971).

because they discriminate against individuals with mental illness, effectively precluding such individuals from being prescribed what often is *the only* effective medication available to treat or control their symptoms.

35. In terms of disparate impact, the current FDA regulations have the effect of discriminating against individuals with mental illness by precluding them from the use of an effective treatment. There is no rational reason why such a prohibition should exist, especially given the fact that FDA-approved medications exist that exhibit a far greater risk of agranulocytosis but which are not subject to a REMS, e.g., the breast cancer drug Ibrance which has an 80% risk of neutropenia.

36. The current FDA regulations governing the use of clozapine are unconstitutional because they constitute an undue burden by placing a substantial obstacle in the path of patients seeking treatment. In *Planned Parenthood of Southeastern Pennsylvania v. Casey*, the Supreme Court defined undue burden as an invalid provision of law whose purpose or effect is to place a substantial obstacle in the path of a patient seeking treatment.[37] The Supreme Court further refined the definition in *Whole Woman's Health v. Hellerstedt*, 136 S. Ct. 2292, 2309 (2016), in which the Court held that it was "wrong to equate the judicial review applicable to the regulation of a constitutionally protected personal liberty with the less strict review applicable [in other contexts]."[38] In other words, the undue burden test is a form of heightened scrutiny that rejects the judicial deference to legislative claims afforded under the rational basis test even if the benefits are minimal or the laws are unnecessary to achieve them. The test articulated in *Whole Woman's Health* has three requirements: 1) the law must actually further a valid state interest; 2) the benefits of the law must outweigh the burdens imposed by the law; and 3) there must be an

[37] *Planned Parenthood of Southeastern Pennsylvania v. Casey*, 505 US 833 (1972).

[38] *Whole Woman's Health v. Hellerstedt*, 136 S. Ct. 2292, 2309 (2016).

evidence-based inquiry based on reliable methodology. While the Supreme Court's holdings were issued in the context of a woman's right to seek an abortion, they are broadly applicable to cases in which laws limit individual rights when their constitutionality depends on whether the law is actually advancing valid interests in a way that justifies the harm placed on the individual.

37. Defendants may argue that the regulations at issue further a valid state interest in that they seek to minimize the number of deaths caused by agranulocytosis. However, two facts undermine the legitimacy of this supposed interest: there is no evidence that discretionary monitoring by the prescribing physician would result in more adverse outcomes, and no other medication with a potential side-effect of agranulocytosis is subject to a REMS monitoring program, even though other FDA-approved medications present an exponentially higher risk than does clozapine. In terms of the benefit/burden analysis, clozapine being a drug of last resort, the target population being among the most volatile and potentially dangerous that exists within society, and the severe and potentially deadly repercussions of cessation of treatment make it clear that the burden imposed by the Clozapine REMS are not outweighed by its benefits. With respect to the third requirement, the Court held that "The statement [] that legislatures, and not courts, must resolve questions of medical uncertainty is also inconsistent with this Court's case law."

38. On January 31, 2020, Defendant Azar declared a nationwide public health emergency as a result of the COVID-19 pandemic.[39] Defendant Azar renewed this declaration

[39] U.S. Department of Health and Human Services (January 31, 2020). Determination that a Public Health Emergency Exists. Available at https://www.phe.gov/emergency/news/healthactions/phe/Pages/2019-nCoV.aspx (Last accessed November 4, 2020.)

again on April 21, 2020[40] and on July 25, 2020[41] and on October 2, 2020[42]. In light of this declaration, on March 22, 2020, the FDA effected a "temporary policy" for certain REMS requirements for the duration of the public health emergency.[43] This policy suspended the mandatory testing requirements for clozapine patients, deferring instead to the medical judgment of health care providers.[44] Given the fact that Defendants have recognized that the medical judgment of health care providers regarding the need for ANC and WBC testing for clozapine patients for the duration of the declared public health emergency, it follows that the mandatory blood testing requirement of the Clozapine REMS is wholly unwarranted.

39. Indeed, it has been infeasible for many patients who would benefit from treatment with clozapine to travel, either for lack of transportation or due to the distance they would need to travel, for their weekly or bi-weekly blood tests.

40. The Clozapine REMS constitutes an impermissible interference with Plaintiff's relationship with his patients, and further constitutes the unauthorized practice of medicine by the FDA. The stopping of a prescription is a medical order. Even if issued by an FDA doctor licensed in the state of the patient, it would be an order issued without examination of the patient.

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[40] U.S. Department of Health and Human Services (April 21, 2020). Renewal of Determination That A Public Health Emergency Exists. Available at https://www.phe.gov/emergency/news/healthactions/phe/Pages/covid19-21apr2020.aspx (Last accessed November 4, 2020.)

[41] U.S. Department of Health and Human Services (July 23, 2020). Renewal of Determination That A Public Health Emergency Exists. Available at https://www.phe.gov/emergency/news/healthactions/phe/Pages/covid19-23June2020.aspx (Last accessed November 4, 2020.)

[42] U.S. Department of Health and Human Services (July 23, 2020). Renewal of Determination That A Public Health Emergency Exists. Available at https://www.phe.gov/emergency/news/healthactions/phe/Pages/covid19-2Oct2020.aspx (Last accessed November 4, 2020.)

[43] U.S. Department of Health and Human Services, Food and Drug Administration (March 2020). Policy for Certain REMS Requirements During the COVID-19 Public Health Emergency. Available at https://www.fda.gov/media/136317/download (Last accessed November 4, 2020.)

[44] *Id.* at p. 7.

A medical order without any evaluation of the patient is a completely unacceptable form of quackery and medical malpractice.

41. The Clozapine REMS discriminates on the basis of gender, with 20% more males than females being subjected to the Clozapine REMS monitoring requirements.

PARTIES

42. Plaintiff David Behar, M.D., is a resident of Pennsylvania and is a board-certified psychiatrist with hundreds of former and dozens of current clozapine patients.

43. Defendant HHS is a federal executive agency, and Defendant FDA is a constituent agency within HHS.

44. Defendant Stephen M. Hahn, M.D., is the Commissioner of Food & Drugs, who is the lead officer within the FDA. He is being sued in his official capacity only. He is responsible for supervising the activities of the FDA, including with regard to the imposition or removal of a REMS.

45. Defendant Alex M. Azar II is the Secretary of Health and Human Services, who is the lead officer within HHS. He is being sued in his official capacity only. He is responsible for administering and enforcing the FD&C Act. In particular, the Secretary is responsible for determining, in consultation with the office responsible for reviewing a drug and the office responsible for post-approval safety with respect to a drug, whether a REMS "is necessary to ensure that the benefits of the drug outweigh the risks of the drug . . ." 21 U.S.C. § 355-1(a)(1). The Secretary may also, in consultation with the office responsible for reviewing the drug and the office responsible for post-approval safety with respect to the drug, require that any REMS include such ETASU as are necessary based on the drug's "inherent toxicity or potential

harmfulness." *Id.* § 355-1(f)(1). The Secretary of HHS has delegated to the FDA the authority to administer the relevant provisions of the FD&C Act.

JURISDICTION AND VENUE

46. This action arises out of Defendants' ongoing violations of the equal protection component of the Due Process Clause, U.S. CONST. amend. V, cl. 4, Section 564 of the Federal Food, Drug and Cosmetic Act ("the FD&C Act"), 21 U.S.C. § 369bbb-3, the Administrative Procedure Act ("APA"), 57 U.S.C. §§ 701-706, and the Americans with Disabilities Act Amendments Act of 2008, 42 U.S.C. § 12101 *et seq.*, and thus raises federal questions over which this Court has jurisdiction pursuant to 28 U.S.C. § 1331 and 1343. This Court also has jurisdiction under 5 U.S.C. § 702 as this is a civil action seeking judicial review of a final agency action, and under 28 U.S.C § 1343(a)(4) as this is a civil action to secure equitable or other relief under any Act of Congress providing for the protection of civil rights.

47. Plaintiff and Plaintiff's patients seek remedies under 28 U.S.C. §§ 1651, 2201, 2202, and 1361, 42 U.S.C. §§ 1983 and 1988, Federal Rules of Civil Procedure 57 and 65, and by the inherent equitable powers of this Court.

48. An actual and justiciable controversy exists between Plaintiff and Defendants requiring resolution by this Court. Plaintiff and Plaintiff's patients have no adequate remedy at law.

49. This Court has authority to award costs and attorneys' fees under 28 U.S.C. § 2412.

50. Plaintiff has suffered injury in the form of lost income from approximately 50% of his mental health patients for whom Plaintiff would prescribe clozapine but who refuse such treatment due to the Clozapine REMS blood monitoring requirements. Plaintiff has standing to

represent the interests of his psychiatric patients. *See Penn. Psychiatric Soc'y v. Green Spring Svcs, Inc.*, 280 F. 3d 278, 289-90 (3d. Cir. 2002).

51. Venue is proper in this United States District Court for the Eastern District of Pennsylvania, under 28 U.S.C. § 1391(b) and (e)(1), and 1402(a)(1), because this is a civil action in which Defendants are an agency, or officers of an agency, of the United States, because Defendant HHS resides in this district by virtue of having an office at 801 Market Street, Suite 9700, Philadelphia, PA 19107 and Defendant FDA resides in this district by virtue of having an office at 900 US Custom House, 200 Chestnut Street, Philadelphia, PA 19106, because a substantial part of the events or omissions giving rise to this action occurred in this District, and because Plaintiff and at least one of Plaintiff's patients who has been injured by virtue of Defendants' actions at issue reside in this District.

52. Because this Court has jurisdiction as a threshold matter, the Declaratory Judgment Act, 28 U.S.C. §§ 2201-2202, provides this Court the power to "declare the rights and other legal relations of any interested party . . ., whether or not further relief is or could be sought." 28 U.S.C. § 2201; *accord* FED. R. CIV. P. 57 advisory committee note ("the fact that another remedy would be equally effective affords no ground for declining declaratory relief").

CONSTITUTIONAL AND STATUTORY BACKGROUND

53. The Due Process Clause of the Fifth Amendment includes an equal-protection component that is coextensive with the equal-protection guarantees of the Equal Protection Clause of the Fourteenth Amendment.

54. At a minimum, under those equal protection guarantees, the government cannot treat similarly situated groups or persons differently without a rational basis for doing so.

55. Upon finding an equal-protection violation, a reviewing court's remedy can "level

up" the disparate treatment of the disfavored class.

56. Congress enacted the Pure Food and Drugs Act, ch. 3915, 34 Stat. 768 (1906), under its Commerce Power. In 1938, Congress amended and replaced that Act with the FD&C Act. Pub. L. No. 75-717, 52 Stat. 1040 (1938) (codified, as amended, at 21 U.S.C. §§ 301-399i).

57. In enacting the FD&C Act, Congress was clear that the FD&C Act *does not* define the practice of medicine. *See* S. Rep. No. 74-361 at 3 (1935) (The FD&C Act is "not intended as a medical practice act and [would] not interfere with the practice of the healing art[s]").

58. Section 1557 of the Affordable Care Act prohibits discrimination in health programs and activities by not only recipients of federal funds but also federal agencies:

> [A]n individual shall not, on the ground prohibited under title VI of the Civil Rights Act of 1964 . . ., or section 504 of [the Rehabilitation Act of 1973] . . ., be excluded from participation in, be denied the benefits of, or be subjected to discrimination under, any health program or activity, any part of which is receiving Federal financial assistance, including credits, subsidies, or contracts of insurance, or under any program or activity that is administered by an Executive Agency or any entity established under this title[.]

42 U.S.C. § 18116(a).

59. The entity Defendant FDA is an "Executive Agency" within the meaning of Section 1557 of the Affordable Care Act.

60. Section 504 of the Rehabilitation Act of 1973 provides in relevant part as follows:

> No otherwise qualified individual with a disability in the United States, as defined in section 705(20) of this title, shall, solely by reason of her or his disability, be excluded from the participation in, be denied the benefits of, or be subjected to discrimination under any program or activity receiving Federal financial assistance or under any program or activity conducted by any Executive agency[.]

29 U.S.C. § 794(a).

61. The entity Defendant FDA is an "Executive agency" within the meaning of

Section 504 of the Rehabilitation Act of 1973.

62. As relevant here, the judicial-review provisions of the APA proscribe agency action that is "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2)(A). The APA further bars agency action that is "in excess of statutory jurisdiction, authority, or limitations," *id.* at § 706(2)(C), and directs courts to "hold unlawful and set aside agency action, findings, and conclusions found to be . . . contrary to constitutional right, power, privilege or immunity." 5 U.S.C. § 706(2)(B).

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63. In relevant part, the judicial-review provisions of the APA proscribe agency action that is "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2)(A). The APA further bars agency action that is "in excess of statutory jurisdiction, authority, or limitations," *id.* at § 706(2)(C), and directs courts to "hold unlawful and set aside agency action, findings, and conclusions found to be . . . contrary to constitutional right, power, privilege or immunity." 5 U.S.C. § 706(2)(B).

64. The doctrine of administrative exhaustion does not apply to constitutional violations.

CAUSES OF ACTION

COUNT 1
(Equal Protection)

65. The allegations of paragraphs 1 through 64 are incorporated as though fully set forth herein.

66. The Clozapine REMS violates Plaintiff's and Plaintiff's patients' right to equal protection of the laws under the Fifth Amendment to the United States Constitution by treating Plaintiff and Plaintiff's patients differently from other similarly situated parties and by placing an

undue burden on Plaintiff and Plaintiff's patients without a sufficient state interest.

COUNT 2
(Administrative Procedure Act: Contrary to Constitutional Right)

67. The allegations of paragraphs 1 through 64 are incorporated as though fully set forth herein.

68. The FDA's reauthorization of the Clozapine REMS and other agency action and inaction described herein constitutes final agency action for which Plaintiffs have no other adequate remedy within the meaning of 5 U.S.C. § 704.

69. The FDA's reauthorization of the Clozapine REMS and other agency action and inaction described herein is contrary to Plaintiff's and Plaintiff's patients' constitutional rights, including their rights under the Fifth Amendment to the U.S. Constitution, in violation of 5 U.S.C. § 706(2)(B).

COUNT 3
(Violation of the Americans with Disabilities Act Amendments Act of 2008)

70. The allegations of paragraphs 1 through 64 are incorporated as though fully set forth herein.

71. The Clozapine REMS, facially and as applied, violates the Americans with Disabilities Act Amendments Act of 2008 ("ADAAA"), Pub. L. 110-325. The ADAAA prohibits discrimination on the basis of disability. 42 U.S.C. § 12132 *et seq.*

72. Regulations implementing Title II of the ADAAA provide that a public entity may not, directly or through contractual or other arrangements, utilize criteria or methods of administration "that have the effect of subjecting qualified individuals with disabilities to discrimination on the basis of disability." 28 C.F.R. § 35.130(b)(3)(i).

73. Regulations implementing Title II of the ADAAA further provide that a public

entity "shall not impose or apply eligibility criteria that screen out or tend to screen out an individual with a disability or any class of individuals with disabilities from fully and equally enjoying any service, program, or activity, unless such criteria can be shown to be necessary for the provision of the service, program, or activity being offered." 28 C.F.R. § 35.130(b)(8).

74. Defendants HHS and FDA are public entities.

75. Under the ADAAA, the term "disability" means: "(a) A physical or mental impairment that substantially limits one or more of the major life activities of [an] individual; (b) a record of such an impairment; or (c) being regarded as having such an impairment." 42 U.S.C. § 12102(2).

76. The ADAAA rule defines "mental impairment" to include "[a]ny mental or psychological disorder, such as . . . emotional or mental illness[.]" 28 C.F.R. § 35.108(b)(1)(ii). Examples of "emotional or mental illness[es]" include major depression, bipolar disorder, anxiety disorders (which include panic disorder, obsessive compulsive disorder, and post-traumatic stress disorder), schizophrenia, and personality disorders. 28 C.F.R. § 35.108(d)(2)(iii)(K).

77. All of Plaintiff's psychiatric patients who have been prescribed clozapine or who would benefit from being prescribed clozapine meet the ADAAA's definition of being disabled.

78. As described herein, the Clozapine REMS imposes criteria that screen out or tend to screen out an individual with a disability or any class of individuals with disabilities from fully and equally enjoying access to medication critical for their well-being without such criteria being medically necessary.

79. Consequently, the Clozapine REMS violates the protections of the ADAAA.

COUNT 4
(Administrative Procedure Act: In Excess of Statutory Authority)

80. The allegations of paragraphs 1 through 64 are incorporated as though fully set forth herein.

81. The FDA's reauthorization of the Clozapine REMS and other agency action and inaction described herein constitutes final agency action for which Plaintiffs have no other adequate remedy within the meaning of 5 U.S.C. § 704.

82. The FDA's reauthorization of the Clozapine REMS and other agency action and inaction described herein is in excess of the agency's statutory authority under the FD&C Act, in violation of 5 U.S.C. § 706(2)(C).

COUNT 5
(Administrative Procedure Act: Arbitrary, Capricious, Abuse of Discretion, and Contrary to Law)

83. The allegations of paragraphs 1 through 65 are incorporated as though fully set forth herein.

84. The FDA's reauthorization of the Clozapine REMS and other agency action and inaction described herein constitutes final agency action for which Plaintiffs have no other adequate remedy within the meaning of 5 U.S.C. § 704.

85. The FDA's reauthorization of the Clozapine REMS was not based on any reasoned decision or rational basis, and therefore was arbitrary, capricious, an abuse of discretion, and otherwise not in accordance with law in violation of 5 U.S.C. § 706(2)(A).

86. The FDA's reauthorization of the Clozapine REMS treated similarly situated entities differently without adequate justification, and therefore was arbitrary, capricious, an abuse of discretion, and otherwise not in accordance with law in violation of 5 U.S.C. § 706(2)(A).

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PRAYER FOR RELIEF

WHEREFORE, Plaintiff and Plaintiff's patients respectfully request that the Court enter judgment in their favor and against Defendants, and each of them, and:

1. Declare, pursuant to 28 U.S.C. § 2201, that the Clozapine REMS in its entirety, as set forth above, violates the Fifth Amendment of the United States Constitution; and/or

   a. Declare, pursuant to 28 U.S.C. § 2201, that certain components of the Clozapine REMS violate the Fifth Amendment of the United States Constitution; and/or

   b. Declare, pursuant to 28 U.S.C. § 2201, that the Clozapine REMS in its entirety, as set forth above, violates the Americans with Disabilities Act Amendments Act of 2008; and/or

   c. Declare, pursuant to 28 U.S.C. § 2201, that certain components of the Clozapine REMS violate the Americans with Disabilities Act Amendments Act of 2008; and/or

   d. Declare, pursuant to 28 U.S.C. § 2201, that the Clozapine REMS, in its entirety, as set forth above, violates the Administrative Procedure Act; and/or

   e. Declare, pursuant to 28 U.S.C. § 2201, that certain components of the Clozapine REMS violate the Administrative Procedure Act.

2. Enter an injunction prohibiting Defendants, their employees, agents, and successors in office, from requiring a REMS for clozapine.

3. Remand to the FDA with instructions to remove the Clozapine REMS.

4. Award to Plaintiff costs, expenses, and attorney's fees pursuant to 42 U.S.C. § 1988 and 28 U.S.C. § 2412.

5. Award such other and further relief, including injunctive relief, as may be necessary to effectuate the Court's judgment or as the Court otherwise deems just and proper.

Respectfully submitted,

Dated: November 5, 2020

By:
David Behar, M.D.

Plaintiff In Propria Persona